

## REMARKS

Claims 2-15 and 46-51 are pending in this application. As the Advisory Action dated October 3, 2003 indicated that the amendments presented in the Amendment Pursuant to 37 C.F.R. § 1.116 filed August 22, 2003 were not entered, claims 52-75 which were presented in that Amendment have been indicated as not entered. All amendments are made relative to the last entered amendment.

Applicant notes that the Office Action Summary of the Office Action dated February 26, 2003 does not list claim 46 as pending in the application. Applicants respectfully submit that claim 46 is pending in the application and was included in the rejections of the claims in that Office Action.

Claims 2 and 47 have been amended herein to correct a typographical error so that the claims recite “neural” precursor cells instead of “neuronal” precursor cells. Support for this amendment is found in the specification at, *inter alia*, page 7, lines 15-17. Claims 2 and 47 have also been amended to indicate that the composition comprises “about 100% isolated neural precursor cells.” Support for this amendment is found in the specification at page 18, lines 30-32. Claims 2, 6, 13, 15, and 47 have been amended herein to more clearly claim the invention. Support for these amendments is found, *inter alia*, in the claims as originally filed and generally throughout the specification. Accordingly, no new matter has been added by these amendments.

Claims 4, 5, 7, 14, 49, and 51 have been cancelled herein without prejudice or disclaimer of the subject matter claimed therein for prosecution at a later date.

New claims 76-99 have been added herein. Support for these new claims is found, *inter alia*, in the claims as originally filed, in the sections cited above, and in the specification at page 24, line 20 to page 26, line 33. Accordingly, no new matter has been added by these new claims.

Therefore, after entry of these amendments claims 2-3, 6, 8-13, 15, 46-48, 50, and 76-99 will be pending in the application.

The specification has been amended to correct various obvious typographical errors. Accordingly, no new matter has been added by these amendments.

The Advisory Action indicates that the standing grounds of rejection are maintained for reasons of record. The outstanding rejections are addressed individually below.

**1. *Claims 2-15 and 46-51 are enabled by the specification as filed.***

Claims 2-15 and 46-51 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to provide an enabling disclosure for the claimed cell composition. Applicant respectfully traverses this rejection.

As claims 4, 5, 7, 14, 49, and 51 have been cancelled in this Amendment, Applicant respectfully submits that the rejection has been rendered moot as to the cancelled claims.

The Office Action dated February 26, 2003 states that while being enabling for a composition comprising up to 66% neural precursor cells derived from ES cells, the application does not reasonably provide enablement for a composition comprising from 85% to 100% isolated neural precursor cells as recited in the claims. Applicant respectfully disagrees.

The  $66 \pm 3\%$  value referred to in the specification at page 24, lines 33-38, refers to the fraction of nestin-positive cells detectable five days after plating of ES cell-derived spheres in the absence of growth factors. In these conditions, the ES cell-derived spheres are induced to differentiate. Accordingly, the cell composition at this time point also includes approximately 34% neurons, 30% astrocytes and 6% oligodendrocytes. The percentages add up to greater than 100% because many of the immature GFAP-positive astrocytes still coexpress nestin and so have been counted more than once.

However, the 66% value does not refer to the maximum number of neural precursor cells obtainable in the composition of the present invention. The fraction of

neural precursor cells obtained by the method in Example 2 and in Example 3 typically approaches 100%.

This fact is corroborated by the Declaration of Dr. Bruestle under 37 C.F.R. § 1.132, which was submitted September 5, 2003 as executed. (Applicant notes that paragraph 11 of the executed Declaration of Dr. Bruestle was amended relative to the unexecuted copy submitted with the Amendment filed August 22, 2003 in order to correct an inadvertently made error. Applicant also notes that Dr. Bengzon, whose statement was attached to the Declaration of Dr. Bruestle as Appendix D, worked with Dr. Bruestle in the laboratory of Ron McKay at the National Institute of Neurological Disorders and Stroke.) This Declaration provides data indicating that the undifferentiated, tumorigenic ES cells have been essentially eliminated from the cell compositions of the present invention, and that neural precursor cells have been generated in unprecedented purity approaching 100%. The Declaration of Dr. Bruestle explains that among other indications regarding the purity of the neural precursor cells, experiments were performed in which a cocktail of antibodies was applied to markers of both immature (nestin and A2B5) and differentiated (beta-III-tubulin, GFAP, and 04) neural precursor cells in order to determine the overall purity of the generated neural cells. The data demonstrates that the cell compositions of the present invention contain more than 99% neural cells. (Declaration of Dr. Bruestle, paragraph 17) This higher purity is necessary in order to obtain the non-tumorigenic cell compositions of the present invention.

Thus, Applicant avers that the specification is enabled for a composition comprising more than 99% neural cells. Accordingly, Applicant respectfully requests that this § 112, first paragraph, rejection be reconsidered and withdrawn.

**2. *Claims 2-15 and 46-51, as amended, are definite.***

Claims 2-15 and 46-51 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite in their recitation of “neuronal precursor cells, which have the ability to differentiate to neuronal or glial cells.”

As claims 4, 5, 7, 14, 49, and 51 have been cancelled in this Amendment, Applicant respectfully submits that the rejection has been rendered moot as to the cancelled claims.

Claims 2 and 47 have been amended herein as suggested by the Examiner to recite “neural precursor cells.” It is obvious from the specification that this was a typographical error as the specification indicates at page 7, lines 15-17 that neural precursor cells are “[i]mmature cell[s] of the nervous system which [have] the potential to develop into mature nervous system cells such as neurons and glia (astrocytes and oligodendrocytes)” and the claim clearly indicates that the intended cells have the ability to differentiate to “neuronal cells, glial cells, or combinations thereof.”

Therefore, in view of the amendment, Applicant respectfully requests that this § 112, second paragraph, rejection be reconsidered and withdrawn.

**3. *Claims 2-15 and 46-51, as amended, are novel.***

Claims 2-15 and 46-51 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Okabe *et al.* (1996). Applicant respectfully traverses this rejection.

As claims 4, 5, 7, 14, 49, and 51 have been cancelled in this Amendment, Applicant respectfully submits that the rejection has been rendered moot as to the cancelled claims.

M.P.E.P. § 2131 states that “‘A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.’ *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).”

Applicant notes that the Examiner has acknowledged on page 2 of the Advisory Action dated October 3, 2003, that the cell compositions of Okabe *et al.* (1996) are tumorigenic.

However, the Advisory Action dated October 3, 2003 also alleges that Applicant’s claim language claiming a composition allowing for up to 15% primitive

embryonic cells and reciting “wherein the cell composition is non-tumorigenic” is contradictory given Applicant’s argument that even a small number of undifferentiated or aberrantly differentiated ES cells suffice to cause tumors or foreign tissues in the graft.

Although Applicant does not necessarily agree, in order to facilitate prosecution the claims have been amended to recite a “composition comprising about 100% isolated neural precursor cells.”

Accordingly, Okabe *et al.* does not teach the non-tumorigenic cell compositions of the claimed invention. Thus, as these claims are not anticipated by Okabe *et al.*, Applicant respectfully requests that the rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

### CONCLUSIONS

In view of the arguments set forth above, Applicant respectfully requests reconsideration and reexamination of the above-referenced patent application.

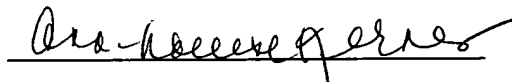
Applicant submits that the rejections contained in the Office Action mailed on February 26, 2003 and the Advisory Action mailed on October 3, 2003 have been overcome, and that the claims are in condition for allowance.

Applicant encloses herewith a Petition for a Three Month Extension of Time pursuant to 37 C.F.R. § 1.136, until January 26, 2004, based on the Notice of Appeal received by the USPTO on August 25, 2003 (January 25, 2004 being a Sunday). Please charge our Deposit Account No. 08-0219 the \$475.00 fee (small entity) for this purpose.

Applicant also herein requests continued examination of the application according to 37 C.F.R. § 1.114. Please charge the same deposit account the \$385.00 fee set forth in 37 C.F.R. § 1.17(e) for this purpose.

No other fees are believed to be due in connection with this response. However, please charge any underpayments or credit any overpayments to Deposit Account No. 08-0219.

Respectfully submitted,



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